REMARKS

A. The Status of the Claims and the Amendments

By the present amendment, claims 30 and 31 have been amended to claim the invention with greater particularity and specificity. The subject matter claimed in new claims 45-64, with respect to treatment of colon cancer, is present in the originally filed specification (see, e.g., paragraph [0080] on page 23 of the original application). No new matter has been introduced in either the new claims or the amended claims. Entry of the amendment is respectfully requested. Upon entry of this amendment, claims 2-6 and 30-64 will remain under consideration.

B. Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 2-6, 20-32, and 34-44 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention (page 2, lines 13-16 of the Office Action). This rejection is respectfully traversed.

The Examiner has stated that the substitutents R_1-R_3 are monovalent radicals that include sulfonyl, which is, according to Examiner, a divalent radical. In the context of the present application, the limitation "sulfonyl" clearly means that the sulfonyl moiety ($-SO_2$) is included within the substitutents R_1-R_3. Claims 30 and 31 have been amended accordingly to include the limitation "substitutents comprising a sulfonyl moiety."

Accordingly, the rejection under 35 U.S.C. § 112, second paragraph, does not apply. It is also submitted that claims 20-29 are currently withdrawn from consideration and therefore should not be rejected until they have been considered. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, are respectfully requested.

C. Rejection Under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 2-6 and 30-44 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which allegedly was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention (the enablement requirement) (page 3, lines 1-6 of the Office Action). This rejection is respectfully traversed on the following grounds.

The Applicants respectfully point out that claims 2-6, 30 (originally as claim 9) and 31 (originally as claim 11) have been before the Examiner from the beginning of the prosecution of this application. Yet, the Examiner has never raised this rejection before. Moreover, in the Office Action dated December 30, 2004 the Examiner has stated that claims 9 and 11 were allowable if re-written in the independent form. Raising this rejection now amounts to piecemeal examination, which is improper. It is well established that an Office Action must be complete as to all maters, and, if a claim is rejected, an examiner is required to provide every valid ground for rejection. See, 37 CFR § 1.104 and also MPEP § 707.07(g).

With respect to the merits of this rejection, the burden of demonstrating that the claims are not enabled is squarely on the Examiner, as required by *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). It is settled law that a presumption of enablement exists, and that ordinarily the lack of enablement rejection should not be given unless there are reasons to doubt the veracity of the statements in the application upon which the reliance for enablement is based. MPEP § 2164.04. It is respectfully submitted that in this case the Examiner has not met the burden of demonstrating the alleged lack of enablement.

The legal standard for determining the adequacy of enablement is well established. To be enabling, "the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation." *Genentech Inc. v. NovoNordisk*, 108 F.3d 1361, 42 USPQ2d 1001 (Fed. Cir. 1997). The Applicants submit that the

specification does comply with the enablement requirement since no undue experimentation is needed to practice the methods recited in claims 2-6 and 30-44.

Specifically, claims 2-6 and 30-44 are directed to pharmaceutical compositions and to articles of manufacture containing such compositions, the compositions including using a compound of formula (I). Claims 31-44, as amended, no longer recite the limitation "useful for inhibiting proliferation of hyperproliferative mammalian cells." The specification clearly provides what compound is to be used in the pharmaceutical composition and what diseases (i.e., cancers) can be treated using the formulation. Example 2 specifically points out that the formulation is particularly effective for the treatment of colon cancer.

It is submitted that, at the most, to enable those having ordinary skill in the art to practice the invention it is necessary to specifically name the compound to be used for treatment, and to specify the symptoms for which the treatment is appropriate. No more is required to enable the claims. The dosage can be established through simple experimentation.

The Examiner has stated that the only direction or guidance provided by the specification is the data for inhibition colon cancer cells (page 5, lines 13-15 of the Office Action). The Examiner has also stated that it would take undue quantity of experimentation to determine what hyperproliferative diseases could be treated (page 5, bottom paragraph through page 6, lines 1-4 of the Office Action).

The Applicants respectfully disagree. The application describes treatments of lung cancer, melanoma, prostate, ovarian cancer, etc. (see, page 13, paragraph [0049] of the specification). The application further provides that the compounds of the invention can be used in combination with other anti-cancer agents (see, pages 14-15, paragraph [0051] of the specification). Since it is known in the art which types of cancer can be treated using the listed anti-cancer compounds, those skilled in the art can easily determine that similar types of cancer can be treated using the compounds of the present invention.

Finally, the Applicants respectfully point out that it is only the necessity of undue experimentation that may make a specification non-enabling. Modest, reasonable quantity of experimentation is allowed, if it is routine or if the specification provides enough guidance. *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). It has never been the rule that the specification itself must necessarily describe how to use every possible variant of the claimed invention. Indeed, "the artisan's knowledge of the prior art and routine experimentation can often fill gaps, interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments." *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003).

Applying these principles to the facts of the present case, it is clear that since the specification provides enough guidance with respect to colon cancer, practicing the invention for treatment of other cancers would require no more than minor variations of what is described, such as adjusting the dosages and the like, which are not more than common tasks routinely performed by competent physicians. Accordingly, the Applicant respectfully submits that the specification properly enables claims 2-6 and 30-44. Reconsideration and withdrawal of the rejection are respectfully requested.

D. Rejection Under 35 U.S.C. § 103 (a)

Claims 31-44 have been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Fenical et al. (WO 02/47610) (last paragraph, page 7 of the Office Action). This rejection is respectfully traversed on the following grounds.

First, the Applicants respectfully point out that the document 02/47610 is not a newly discovered reference. In fact, the Examiner considered and used this reference in the previous Office Action against claims 2-6, 23, and 24 as a 102(a) reference and against claims 8, 25, and 26 as a 103(a) reference (see, the Office Action mailed 12/30/04, page 3, lines 11-13, and page 4, lines 1-2). At the same time, the Examiner clearly stated that claims 9 and 11 will be allowable

(i.e., novel and non-obvious over the document 02/47610) so long as they are re-written in independent form including all the limitations of the base and the intervening claims.

The Applicants have re-written claims 9 and 11 accordingly, and provided them in the amendment filed May 31, 2005, where claim 11 was presented in independent form as claim 31. It is, therefore, unclear, why the Examiner has rejected this claim over the reference she had had before her previously, in view of her conclusion of allowability of this claim. The Applicants would greatly appreciate if the Examiner should elucidate her position. Otherwise, such rejection will amount to piecemeal examination, which, as discussed above, is improper.

Second, it is axiomatic that to establish a prima facie case of obviousness, the following three basic criteria must be met: (1) there must be some suggestion or motivation to modify the reference as proposed by the Examiner; (2) there must be a reasonable expectation of success and (3) the prior art reference must teach or suggest all of the claim limitations. MPEP § 2143. The Applicants submit that at least one of the above criteria have not been met.

Claim 31 is directed to a pharmaceutical composition that includes compound (I) "and further comprising at least one additional anti-neoplastic agent." The 02/47610 reference mentions that Salinosporamide A is an anti-cancer agent, but is silent with respect to compositions containing both this agent and at least one other anti-neoplastic agent, other than Salinosporamide A. The Examiner has stated that one skilled in the art will be motivated to prepare a compositions containing the compound of the invention (page 8, lines 13-15 of the Office Action). However, the Examiner has not demonstrated that that one skilled in the art will be also motivated to include an additional anti-neoplastic agent in the composition. It is submitted that there is no such motivation or suggestion because the 02/47610 reference is silent with respect to potential compositions.

Accordingly, it is submitted that claim 31 is patentably distinguishable over the 02/47610 reference. Claims 32-44 depend, directly or indirectly on claim 31 and are considered patentable

for at least the same reason. In view of the foregoing, reconsideration and withdrawal of the rejection of claims 31-44 under 35 U.S.C. § 103(a), are respectfully requested.

E. Other Objections

The Examiner objected to the specification and asked to supply the missing ATCC Accession Numbers in paragraphs [0012] and [0040]. The ATCC Accession Number for the strain CNB476 (PTA-5275) was added to the specification by the preliminary amendment filed April 30, 2004. The strain CNB392 is identical to the strain CNB476, as evidenced by the Declaration of an inventor, which is attached herewith. Therefore, it is unnecessary to provide a separate ATCC Accession Number. The specification has been now amended accordingly. Accordingly, the objection has become moot. Reconsideration and withdrawal of the objection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

Check No. 580923 in the amount $960.00 to cover fees for additional claims over twenty (18 total ;$450.00) and the Three-Months Extension of Time ($510.00) fee is attached herewith. No other fees are believed due in connection with this Response. In the event that an additional fee is due, the Commissioner is hereby authorized to charge any amounts required by this filing, or credit any overpayment, to Deposit Account No. 07-1896.

Respectfully submitted,

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Victor Regis reg 45,039

for Lisa A. Haile, J.D., Ph.D.
Registration No. 38,347
Telephone: (858) 677-1456
Facsimile: (858) 677-1465

DLA PIPER RUDNICK GRAY CARY US LLP
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133
USPTO Customer Number 28213